

3

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Pieraccioli, D.  
ISTITUTO FARMACOLOGICO SERONO SPA  
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ITALIE

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year)

19.10.99

Applicant's or agent's file reference  
WO/360/A

## IMPORTANT NOTIFICATION

International application No.  
PCT/EP98/06143

International filing date (day/month/year)  
28/09/1998

Priority date (day/month/year)  
29/09/1997

Applicant

APPLIED RESEARCH SYSTEMS et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

## 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.



European Patent Office - P.B. 13619 Patentaan  
NL-2220 HV Rijswijk - Pays Bas  
Tél. 01 73 31 20 20 - Tél. 01 73 31 20 20

Dekker, M.



## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicants or agent's file reference WO/360/A	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP98/06143	International filing date (day/month/year) 28/09/1998	Priority date (day/month/year) 29/09/1997
International Patent Classification (IPC) or national classification and IPC C12N15/19		
Applicant APPLIED RESEARCH SYSTEMS et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand

Date of completion of this report

International Preliminary Examining Authority



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Hix R



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP98/06143

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-23 as originally filed

**Claims, No.:**

1-14 as originally filed

**Drawings, sheets:**

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ neither restricted nor paid additional fees.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP98/06143

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
- ☒ not complied with for the following reasons:

**see separate sheet**

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☒ all parts.
- ☐ the parts relating to claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP98/06143

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**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**Re Item IV**

**Lack of unity of invention**

The IPEA agrees with the objection put forward by the ISA as to lack of unity, the reasons for the objection being as follows:

The prior art D1: J. Exp. Med. vol. 181, February 1995, pages 631-640, J-H. Gong et al. discloses several truncated analogues of the C-C chemokine MCP-1 including 8-76, 9-76 and 10-76 which were not significantly active, however these analogues were antagonists of MCP-1 activity with the most potent being the 9-76 analogue and MCP-1 {3-76} being less potent.

D11: Nature, vol. 383, 3 October 1996, page 400, F. Arenzana-Selsdedos et al. describes the synthesis of a RANTES chemokine with the first eight amino-terminal amino acids deleted, termed RANTES{9-68}. The analogue lacked chemotactic and leukocyte-activating properties and acted as a receptor antagonist.

In view of the state of the art the problem may therefore be defined as the provision of alternative chemokines exhibiting antagonistic activity and an alternative means to truncate the chemokines at the amino-terminus.

The present application provides the following solutions;

- 1.) truncation of the chemokine RANTES at the amino terminus up to 4 amino acids and
- 2.) the use of CD/DPP IV to generate the NH<sub>2</sub>-terminally truncated chemokines in vitro.

Due to the fact that synthetically produced NH<sub>2</sub>-terminally truncated RANTES chemokines are known in the state of the art, due to the fact that the different solutions are essentially different in terms of solution 1 provides the result and solution 2 provides the means and due to the absence of further technical features which could provide a common novel and inventive linking concept, the IPEA is of the opinion that there is no single inventive concept underlying the set of claimed inventions of the present application according to Rule 13.1 PCT.

There is therefore lack of unity and the different inventions, not belonging to a common inventive concept are formulated as the following different subjects according to Article 17{3}{a} PC;

1. Claims 1 to 12 :

Amino-terminal truncated C-C chemokine, **RANTES**, having chemokine antagonistic activity, DNA molecules encoding said chemokine, expression vector comprising said DNA, host cell comprising said vector, recombinant process for preparing said protein, said chemokine used as a medicament and pharmaceutical compositions comprising said protein.

2. Claims 13 and 14 :

Use of CD26/DPP IV in the therapy and/or diagnosis of the diseases, in which an antagonistic activity of the chemokine effects is required.

Re Item V

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following documents are considered in this report;

- DI : J. Exp. Med. vol. 181, February 1995, pages 631-640, J-H. Gong et al.  
DII : Nature, vol. 383, 3 October 1996, page 400, F. Arenzana-Selsdedos et al.  
DIII : Journal of Immunological Methods. vol. 189, 1996, pages 99-105,  
I. De Meester et al.

I. Substantive examination on the following subject-matter;

1. Claims 1 to 12 : Amino-terminal truncated C-C chemokine, **RANTES**, having chemokine antagonistic activity, DNA molecules encoding said chemokine, expression

1.) The prior art DI discloses several truncated analogues of the C-C chemokine MCP-1 including 8-76, 9-76 and 10-76 which were not significantly active, however these analogues were antagonists of MCP-1 activity with the most potent being the 9-76 analogue and MCP-1 {3-76} being less potent. DII describes the synthesis of a RANTES chemokine with the first eight amino-terminal amino acids deleted, termed RANTES{9-68}. The analogue lacked chemotactic and leukocyte-activating properties and acted as a receptor antagonist.

2.) The present application provides the chemokine RANTES truncated at the amino terminus up to 4 amino acids and having a chemokine activity, DNA molecules encoding said peptides, expression vectors comprising said DNA and host cells comprising said expression vector.

2.1) Amino-terminally truncated RANTES according to the present application and exhibiting a chemokine activity are not disclosed in the state of the art. The subject-matter of Claims 1 to 12 is therefore novel according to Article 33{2} PCT.

2.2) In view of the state of the art the problem may therefore be defined as the provision of alternative chemokines exhibiting antagonistic activity.

2.3) The present application provides the solutions of truncating the chemokine RANTES at the amino terminus up to 4 amino acids.

2.4) Amino-terminally truncated C-C chemokines are known in the state of the art: MCP-1{8-76, 9-76 and 10-76} from DI and RANTES{9-68} from DII and although the MCP-1{3-76} analogue is less potent than the other truncated analogues disclosed in DI, nevertheless MCP-1{3-76} still appears to exhibit a chemokine antagonistic activity.

2.4) The examples of the application demonstrate that the RANTES{3-68} clearly exhibits chemokine antagonistic activity. There is no suggestion nor indication in the

EXAMPLES OF AMINO-TERMINAL RANTES{3



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP98/06143

2.5} Consequently the subject-matter of Claims 1 to 12, involving the RANTES lacking amino acids 1-2 at the NH<sub>2</sub>-terminal, RANTES{3-68}, appears to satisfy the criteria of novelty and inventive step according to Articles 33{2} and {3} PCT.

II. Substantive examination on the following subject-matter;

2. Claims 13 and 14: Use of CD26/DPP IV in the therapy and/or diagnosis of the diseases, in which an antagonistic activity of the chemokine effects is required.

1.} DIII discloses the purification of CD26/dipeptidyl peptidase IV {CD/DPP IV} and the demonstration that it cleaves off the N-terminal dipeptides from peptides when a proline or alanine is located at the penultimate position. DIII neither discloses the use of CD/DPP IV in therapy and/or diagnosis of the diseases in which an antagonistic activity of the chemokine effects is required, nor the treatment of inflammatory, immune and infectious diseases.

1.1.} The subject-matter of Claims 13 and 14 is clearly novel according to Article 33{2} PCT.

2.} In the light of the prior art DI and DII, the problem may therefore be defined as the provision an alternative means to truncate the chemokines at the amino-terminus.

2.1} The solution of using CD/DPP IV as a means to amino-terminally truncate chemokines which may then be used in therapy and/or diagnosis of the diseases in which an antagonistic activity of the chemokine effects is required and in the treatment of inflammatory, immune and infectious diseases is not suggested in the state of the art.

2.2} Consequently the use of CD/DPP IV according to Claims 13 and 14 is considered to involve an inventive step according to Article 33{3} PCT.

**Re Item VII**

**Certain defects in the international application**

Page 3 of 4

**Re Item VIII**

**Certain observations on the international application**

1.} There is no evidence that a RANTES truncated at the NH<sub>2</sub>-terminal and lacking more than 2 amino acids would still exhibit a chemokine antagonistic activity. The assertion of Claim 1 that amino-terminally truncated RANTES, lacking the NH<sub>2</sub>-terminal amino acids corresponding to amino acids 1-3 or 1-4 and still exhibiting a chemokine antagonistic activity appears to be purely speculative, not based on any technical facts or evidence and not supported by the description.

1.1} The subject-matter of Claim 1 is therefore considered to encompass subject-matter that is not demonstrated as involving an inventive step and not supported by the description according to Article 6 PCT.

1.2} The Applicant is requested to limit the independent Claim 1 to subject-matter that is recognised as involving an inventive step, ie. the subject-matter of Claim 2 defining RANTES{3-68}.

2.} The abbreviation "CD/DPP IV" must be defined as "CD26/dipeptidyl peptidase IV" in Claim 13, to avoid ambiguity and for the sake of the clarity of the claims, according to Article 6 PCT.

3.} According to the description page 6, lines 18 to 29, CD/DPP IV is able to generate amino-terminally truncated RANTES in vitro. The wording of Claims 13 and 14 is considered to be rather ambiguous because according to the description it appears that the amino-terminally truncated RANTES generated by the CD/DPP IV are used in the therapy and/or diagnosis of disease, whereas according to the Claims 13 and 14 the CD/DPP IV itself is used in the therapy and/or diagnosis of disease. Claims 13 and 14 are therefore unclear according to Article 6 PCT.

3.1} In addition the description states that "RANTES is the first cytokine reported whose biological activity is modified by CD/DPP IV", whereas Claim 13 implies that CD/DPP IV

## PCT

### NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

PIERACCIOLI, Daniele  
Istituto Farmacologico Sersono  
S.p.A.  
Via Casilina, 125  
I-00176 Rome  
ITALIE

<b>Date of mailing (day/month/year)</b> 13 December 1999 (13.12.99)	
<b>Applicant's or agent's file reference</b> WO/360/D	<b>IMPORTANT NOTIFICATION</b>
<b>International application No.</b> PCT/EP98/06143	<b>International filing date (day/month/year)</b> 28 September 1998 (28.09.98)

1. The following indications appeared on record concerning:

☒ the applicant
 ☐ the inventor
 ☐ the agent
 ☐ the common representative

Name and Address

APPLIED RESEARCH SYSTEMS  
Ars Holding N.V.  
John B. Gorsiraweg 14  
Curacao  
Netherlands Antilles

State of Nationality

NL

State of Residence

NL

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person
 ☐ the name
 ☒ the address
 ☐ the nationality
 ☐ the residence

Name and Address

APPLIED RESEARCH SYSTEMS ARS  
HOLDING N.V.  
Pietermaai 15  
Curaçao  
Netherlands Antilles

State of Nationality

NL

State of Residence

NL

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office
 ☐ the designated Offices concerned  
☐ the International Searching Authority
 ☒ the elected Offices concerned

International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

003009288

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International Bureau



PTO

0554537858



03/28/00

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>C12N 15/19, C07K 14/52, A61K 38/19, 38/48, G01N 33/68</b>		<b>A1</b>	(11) International Publication Number: <b>WO 99/10537</b>
			(43) International Publication Date: 8 April 1999 (08.04.99)
(21) International Application Number: PCT/EP98/06143			<b>(81) Designated States:</b> AU, BG, BR, CA, CN, CZ, EE, HU, IL, JP, KP, KR, MX, NO, NZ, PL, SG, SK, UA, US, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(22) International Filing Date: 28 September 1998 (28.09.98)			
(30) Priority Data: 97116863.8      29 September 1997 (29.09.97)      EP 97122471.2      19 December 1997 (19.12.97)      EP 98104216.1      10 March 1998 (10.03.98)      EP			
(71) Applicant (for all designated States except US): <b>APPLIED RESEARCH SYSTEMS [NL/NL];</b> Ars Holding N.V., John B. Gorsiraweg 14, Curacao (AN).			
(72) Inventors; and (75) Inventors/Applicants (for US only): <b>PROOST, Paul [BE/BE];</b> W. Van den Abeelaan 21, B-3001 Heverlee-Leuven (BE); <b>STRUYF, Sorie [BE/BE];</b> Molenaarstraat 66, B 2841 Rumst (BE); <b>VAN DAMME, Jo [BE/BE];</b> Tintorettostraat 32, B-1000 Brussels (BE).			
(74) Agent: <b>PIERACCIOLI, Daniele;</b> Istituto Farmacologico Sersono S.p.A., Via Casilina, 125, I-00176 Rome (IT).			

(54) Title: **AMINO-TERMINALLY TRUNCATED RANTES AS CHEMOKINE ANTAGONISTS**

(57) Abstract

The present invention relates to amino-terminally truncated RANTES, lacking NH<sub>2</sub>-terminal amino acids corresponding to amino acid residues 1, 1-2, 1-3 or 1-4 of the naturally-occurring RANTES and having chemokine antagonistic activity, as well as cDNA sequences encoding them, their use in therapy and/or in diagnosis of the diseases, in which an antagonistic activity of the chemokine effects is required, and pharmaceutical compositions comprising them.

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>W0/360/D</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 98/ 06143</b>	International filing date (day/month/year) <b>28/09/1998</b>	(Earliest) Priority Date (day/month/year) <b>29/09/1997</b>
Applicant <b>APPLIED RESEARCH SYSTEMS et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).

2. ☒ Unity of invention is lacking (see Box II).

3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

☒ filed with the international application.

☐ furnished by the applicant separately from the international application.

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the **title**, ☒ the text is approved as submitted by the applicant

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claim : 1 to 12

Amino-terminal truncated C-C chemokine, RANTES, lacking the NH<sub>2</sub>-terminal amino acids corresponding to amino acid residue 1, 1-2, 1-3 or 1-4 of the naturally occurring RANTES and having chemokine antagonistic activity, DNA molecules encoding said chemokine, expression vector comprising said DNA, host cell comprising said vector, recombinant process for preparing said protein, said chemokine used as a medicament and pharmaceutical compositions comprising said protein.

2. Claim : 13 and 14

Use of CD26/DPP IV in the therapy and/or diagnosis of the diseases, in which an antagonistic activity of the chemokine effects is required.

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/19 C07K14/52 A61K38/19 A61K38/48 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K C12N A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GONG J-H ET AL: "RANTES and MCP -3 antagonists bind multiple chemokine receptors." JOURNAL OF BIOLOGICAL CHEMISTRY 271 (18). 1996. 10521-10527. ISSN: 0021-9258, XP002047804 cited in the application see table 1 ---	1-12
A	F. ARENZANA-SELSOEDOS ET AL.: "HIV blocked by chemokine antagonist." NATURE, vol. 383, 3 October 1996, page 400 XP002027718 see the whole document --- -/--	1-12



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"S" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

Address of the

European Patent Office, P.O. Box 1, Patentstrasse 1  
NL - 2280 HV Rijswijk  
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Fax: (+31-70) 340-3016

Hix, R



## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BAGGIOLINI M ET AL: "HUMAN CHEMOKINES: AN UPDATE" ANNUAL REVIEW OF IMMUNOLOGY, vol. 15, 1997, pages 675-705, XP002055737 see the whole document ---	1-12
T	T. ORAVECZ ET AL.: "Regulation of the receptor specificity and function of the chemokine RANTES {Regulated on Activation, Normal T Cell Expressed and Secreted} by Dipeptidyl Peptidase IV {CD26}-mediated cleavage." THE JOURNAL OF EXPERIMENTAL MEDICINE, vol. 186, no. 11, 1 December 1997, pages 1865-1872, XP002056059 see the whole document ---	1-12
A	WO 96 17935 A (GLAXO GROUP LTD ;WELLS TIMOTHY NIGEL CARL (CH); PROUDFOOT AMANDA E) 13 June 1996 see the whole document ---	
A	A.E.I. PROUDFOOT ET AL.: "Extension of recombinant human RANTES by the retention of the initiating methionine produces a potent antagonist" THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 5, 2 February 1996, pages 2599-2603, XP002056060 cited in the application see the whole document ---	
A	I. DE MEESTER ET AL.: "Use of immobilized adenosine deaminase {EC 3.5.4.4} for the rapid purification of native human CD26/dipeptidyl peptidase IV {EC3.4.14.5}" JOURNAL OF IMMUNOLOGICAL METHODS, vol. 189, 1996, pages 99-105, XP002056062 cited in the application see the whole document -----	13,14

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
W0 9617935 A	13-06-1996	AU 688641 B	12-03-1998
		AU 4120896 A	26-06-1996
		BR 9509890 A	30-12-1997
		CA 2207036 A	13-06-1996
		CN 1168697 A	24-12-1997
		CZ 9701719 A	12-11-1997
		EP 0796330 A	24-09-1997
		FI 972433 A	06-06-1997
		HU 77075 A	02-03-1998
		JP 10510151 T	06-10-1998
		NO 972620 A	06-08-1997
		NZ 296570 A	25-11-1998
		PL 320565 A	13-10-1997

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